

# Characterization of platelet disorders using quantitative proteomics

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Stellingen behorende bij het proefschrift:

*Characterization of platelet disorders using quantitative proteomics*

1. In spite of continuous improvements in the field of phosphoproteomics, major challenges are still the poor behavior of multiply phosphorylated peptides during chromatography and LC-MS as well as the determination of phosphorylation stoichiometries. *This thesis*
2. The charge-based fractional diagonal chromatography (ChaFRADIC) workflow combined with iTRAQ labeling is a powerful, reproducible and sensitive method to investigate proteolytic processes in human cells, such as platelets. *This thesis*
3. Parallel reaction monitoring (PRM), as an alternative for immunoassays, is useful to validate quantitative changes of characteristic phosphorylation sites in (ant)agonist-regulated platelet proteins. *This thesis*
4. A combination of functional analysis and quantitative proteomics data is needed for the proper understanding of platelet dysfunction in patients with bleeding disorders. *This thesis*
5. A limitation of very rare disorders such as the Scott syndrome is that, even when multiple blood samples from the same patient are available, generalization of the findings relies on evidence obtained from non-patient studies. *This thesis*
6. Multi-omics approaches - using parallel studies of proteins, lipids and metabolites - applied to a human cell or tissue sample, are powerful for obtaining a deeper knowledge of the healthy or diseased state of the subject.
7. Multiple developments have contributed to the success of *bottom-up proteomics* research. These include methods to fractionate complex peptides mixtures, next generation mass spectrometers, advanced quantification methods, and improved bioinformatics approaches to analyze and assemble complex data sets.
8. The analysis of intact proteins in a mass spectrometer (*top-down proteomics*) allows the characterization of proteoforms and post-translational modifications without inference problems of peptide-based proteomics.
9. Valorization and industrialization of proteomics and bioinformatics approaches can transform the future of healthcare, by opening a plethora of advantages including personalized medicine.
10. A peaceful spirit is a wonderful guide for a doctoral student to choose the right research topic.
11. Success is a science; if you have the conditions, you get the result. *Oscar Wilde*

Fiorella Andrea Solari, 26<sup>th</sup> June 2018